Transporting Newly Sequenced Polypeptides

Although cell biologists' tools of electron microscopy and cell fractionation played important roles in unraveling the mechanism through which different types of RNA contributed to protein synthesis, cell biologists were also interested in the fate of newly formed proteins. Utilizing C^{14} labeling in pancreatic microsomes from pigeons, Colvin Redman, Siekevitz, and Palade (1966) found evidence that labeled amylase, the secretory protein being synthesized, would appear in the cisternal cavities of the microsome. Subsequent research by Redman and David Sabatini (1966) demonstrated that treating the ribosome with puromycin resulted in the appearance of labeled unfinished proteins in the cisternal cavities. They viewed this as showing that "from the onset of protein synthesis the growing peptide chain is directed towards the cisternal space into which it diffuses upon its release from the attached ribosome" (p. 608). Earlier research by Sabatini (Sabatini et al., 1966) had demonstrated that it was the large ribosomal subunit that was directly attached to the membrane of the endoplasmic reticulum, leading to the conclusion that the new protein was transported from the large subunit through the membrane to the cisternal space. Palade, in his 1974 Nobel Lecture, noted that the vectorial transport of newly formed proteins into the cisternal space provided the only known explanation for the complex structure of the endoplasmic reticulum:

> This conclusion provides a satisfactory explanation for the basic structural features of the endoplasmic reticulum: a cavitary cell organ of complicated geometry which endows it with a large surface. All these features make sense if we assume that one of the main functions of the system is the trapping of proteins produced for export. With the exception of Ca^{2+} accumulation in the sarcoplasmic reticulum, i.e., the equivalent cell organ of muscle fibers, no other recognized function of the endoplasmic reticulum (e.g., phosphatide and triacylglycerol synthesis, mixed function oxygenation, fatty acid desaturation) requires compellingly and directly a cavitary organ, at least according to our current knowledge. (Palade, 1992, p. 183)

As we will see, the next stage in the movement of the newly formed proteins was to the Golgi apparatus, and this discovery led Palade to reverse his earlier denial of the reality of the Golgi and to conduct landmark studies on its function.

3. TWO ADDITIONAL ORGANELLES

Research in the 1950s and early 1960s on the mitochondrion and the endoplasmic reticulum resulted in the first mechanistic models of cellular functions.